REMARKS

1. Restriction Requirement:

Applicant appreciates the Examiner's acknowledgement of Applicant's election of Group I and affirms the same.

2. Rejection of Claims 32-34 under 35 U.S.C. 112, first paragraph

The Examiner rejected claims 32-34 under 35 U.S.C. 112, first paragraph for the reasons of record. Specifically, the Examiner stated that the Applicant has not disclosed how one skilled in the art can use the method of detecting changes in lipid phosphatase activity and correlating these changes to disease detection.

By way of the foregoing, Applicant has amended Claim 32 in response to the rejection.. The claim now includes a limitation directed to change detection., Support for the amendment is found at page 3, line 24, where it is disclosed that SHIP1 is a 5' lipid phosphatase which converts $PI(3,4,5)P_3$ to $PI(3,4)P_2$. On page 4, line 1, of the specification, it states that ablation of SHIP1 in transgenic mice lead to chronic hyperplasia and increased proliferation and survival of hematopoetic cells. As such, one of ordinary skill in the art would understand from this disclosure that as a phosphatase activity slows or is removed, the rate of conversion of $PI(3,4,5)P_3$ to $PI(3,4)P_2$ slows or stops, which in turn leads to elevated levels of $PI(3,4)P_2$. Elevated levels of $PI(3,4)P_2$ due to changes in phosphatase activity correlate with chronic hyperplasia, etc.

Further, on page 4, line 18 of the specification, it states that "elevated $PI(3,4,5)P_3$ levels contribute to cancer progression..." On that same page at line 31, it explains that "by converting $PI(3,4,5)P_3$ to $PI(4,5)P_2$, PTEN acts as a negative regulator of PKB/Akt activation. As such, one skilled in the art would understand from this disclosure that as a phosphatase activity slows, the rate of conversion of $PI(3,4,5)P_3$ to $PI(4,5)P_2$ would also slow, thus correlating to cancer progression.

As another example of how the specification enables one of ordinary skill in the art to use the instant invention, page 6, line 30, explains that $PI(3,4,5)P_3$ has been pinpointed as the major mediator of the PI 3-K dependent insulin response. Line 32 of that same page reads, "thus, modulation of $PI(3,4,5)P_3$ levels by phosphoinositide phosphatase activity is important

in the signaling pathways governing insulin-regulated glucose metabolism, and could provide a possible point of intervention for treatment of NIDDM." In view of the foregoing, one of ordinary skill in the art would understand that since $PI(3,4,5)P_3$ is a major mediator of the PI 3-K dependent insulin response, inactivity of a phosphatase which hydrolyzes $PI(3,4,5)P_3$ would lead to elevated levels of $PI(3,4,5)P_3$ and thus allow for disease detection.

Thus, Applicant respectfully submits that the instant specification provides sufficient examples and guidance related to detecting changes in phosphatase activity and how such changes correlate with the detection of diseases so that one of ordinary skill in the art would be enabled to use the instant invention without undue experimentation. As such, Applicant respectfully requests withdrawal of the rejection of claims 32-34 under 35 U.S.C. 112, first paragraph.

3. Rejection of Claims 1-4, 7, 8, 10-15, 32-34 and 38 under 35 U.S.C. 112, second paragraph

The Examiner rejected claims 1-4, 7, 8, 10-15, 32-34 and 38 under 35 U.S.C. 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention for the reasons of record. In light of the same, Applicant has amended the claims to more particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Support for the amendments can be found on page 13, lines 20-34, and throughout the application. For example, the assay of certain embodiments of the instant invention is explained in that a phosphoinositide substrate interacts with a phosphatase to form a product lipid. The product lipid is then detected by the detection reagent. In light of the specification and its plain language, it is clear that the lipid phosphatase is exposed to the substrate lipid and the resulting reaction product lipid is detected by a detection reagent.

The Examiner also stated that it is not clear if the solution contains lipid phosphatase. On page 13 of the specification, lines 30-33, it states that the minimal components of a phosphoinositide phosphatase assay of the present invention are 1) a source enzyme, 2) the appropriate phosphoinositide substrate, and 3) a detection reagent. As such, this supports

amended claim 1 and indicates that the solution may contain a source enzyme, e.g. lipid phosphatase.

The Examiner asked if Applicant is performing a method to determine lipid phosphatase activity in a sample or does Applicant merely intend to detect a product lipid. Applicant submits that certain embodiments of the instant invention are capable of detecting a product lipid of a reaction between a phosphatase and substrate lipid. As such, these embodiments are capable of detecting a product lipid. Also, particular embodiments of the instant invention are capable of determining lipid phosphatase activity in a sample. One manner in which this can be accomplished is to run an assay of the instant invention and if no product lipid is detected by the detection reagent, then it may be determined that there is little or no phosphatase activity in the sample.

The Examiner also stated that claim 1 is vague and indefinite because it is unclear what relationship exists between the lipid detector protein and the product lipid or a substrate lipid. Specifically, the Examiner asked if the detector protein binds to the lipid product or does it come in close proximity of the lipid product. Applicant asserts the lipid detector protein binds to the lipid product.

Next, the Examiner argued that the recitation "other lipid-binding domains" in claim 4 is vague and indefinite. Applicant respectfully disagrees with this assertion.

The Examiner's attention is respectfully directed to page 8, line 21, which reads that, "the signaling pathways involving these lipid modifying enzymes..." Applicant asserts that upon reading this disclosure, one of ordinary skill in the art would understand that "other lipid-binding domains" refers to those which are capable of interacting with lipids. Also, one of ordinary skill in the art would understand which particular functional groups need to be present in the domain for a reation or interaction to occur with the lipid. Further, on page 10 lines 3-4 Applicant describes that "...proteins that are specific for $PI(3,4)P_2$ or $PI(4,5)P_2$ can be used in accordance with the invention." Applicant submits that this further supports "other lipid-binding domains" of certain embodiments of the instant invention as one of ordinary skill in the art would clearly understand which domains would be capable of binding or interacting with $PI(3,4)P_2$ or $PI(4,5)P_2$. Since definiteness of a claim must be analyzed in light of the content of the application, Applicant submits that claim 4 clearly sets out the

boundaries of certain embodiments of the instant invention and the subject matter for which protection is sought.

Also, the Examiner stated that claim 12 is vague and indefinite because it is unclear what relationship the additional lipids in the solution have with the substrate lipid, product lipids, lipid detector protein and enzyme. Specifically, the Examiner asked whether the additional lipids bind to the lipid detector, whether they are substrate or product lipids, and whether they have a function in the assay.

Applicant respectfully directs the Examiner's attention to page 10, lines 8-10, wherein the Applicant discloses that, "additional competing and noncompeting lipids can also be present in the solution, enabling the assay method of the present invention to be used with complex solutions..." In light of this disclosure, Applicant submits that the lipids in question may be of any type, may bind to the lipid detector if they are competing lipids, and may not bind to the lipid detector if they are noncompeting lipids. As such, in certain embodiments of the invention, they have a function in the assay and in other embodiments they do not.

Next, the Examiner stated that the use of the acronym "PIPn" in claim 13 is vague and indefinite. Applicant submits that one of ordinary skill in the art would recognize and understand the boundaries contemplated by a molecule with the formula PIPn. Further, Applicant respectfully disagrees with the Examiners statement that the specification does not provide a definition for PIPn. On page 1, line10, the specification discloses "phosphotidylinositol phosphates (PIPns)." One of ordinary skill in the art would understand that phosphotidylinositol phosphates is defining the acronym (PIPn) and (PIPns) is merely a plural form of (PIPn).

Further, the Examiner stated that the recitation "acts on" in claim 13 is vague and indefinite. Applicant respectfully disagrees with this statement. As an example, upon reading page 1 line 8, one of ordinary skill would get a clear definition of what "acts on" refers to in accordance with certain embodiments of the present invention. This portion of the specification explains that "the present invention relates to enzymes that dephosphorylate inositol lipids..." According to this embodiment of the instant invention, one of ordinary skill would understand that "acts on" means dephosphorylates.

Moreover, Applicant would like to clarify that it is the lipid phosphatase of claim 13 that is selected from the group consisting of SHIP1, SHIP2, PTEN, PTPRQ, SKIP, Myotubularin, MTMR2 and OCRL1. These are all listed as examples of phosphatases in the specification. See, for example, page 12, lines 31-32.

Also, the Examiner stated that claim 32 is vague and indefinite because the preamble of the claim does not correlate with the body of the claim. In response to the Examiner's argument, and in order to expedite allowance of claims, Applicant has amended claim 32. Such amendment is made without prejudice or disclaimer of the subject matter therein and solely to expedite prosecution and allowance of the claims. In light of the aforementioned amendment, Applicant respectfully requests withdrawal of the rejection of claims 32 under 35 U.S.C 112, second paragraph.

Next the Examiner stated that the phrase "disease caused alteration of a lipid phosphatase" of claim 32 is vague and indefinite because it is unclear what alteration or how a lipid phosphatase is altered. Applicant submits that the specification provides numerous examples of what an alteration can be. Specifically, see page 4, line 33, through page 5, line 5, describing a loss of the phosphatase activity as an example of an alteration and how this correlates with particular diseases. Further, page 5, lines 6-20, list many references that disclose how a lipid phosphatase may be altered.

The Examiner stated that claim 38 is vague and indefinite because it is unclear how the Applicant is "using" the lipid phosphatase assay of claim 1 to screen a compound having an enhancing or inhibiting effect. Specifically, the Examiner asked if the assay recited in claim 1 provides information for comparisons to determine an enhancing or inhibiting effect.

Applicant respectfully directs the Examiner's attention to page 9, lines 21 – 24, which explain that exposing a lipid detector protein containing a lipid recognition motif with a binding specificity for a product lipid of a lipid phosphatase, to a solution containing a substrate lipid of said lipid phosphatase; and determining whether said product lipid is present in said solution. Applicant asserts page 9, lines 21 – 24, clearly teach how to use the assay of particular embodiments of the instant invention to detect changes in the lipid phosphatase activity. Specifically, one of ordinary skill would understand that upon running the assay of certain embodiments of the instant invention, if there is no product lipid detected, then the

activity of the phosphatase has potentially been lost. This is merely one example of how the assay can be used to detect changes in a phosphatase activity.

As such, Applicant respectfully requests withdrawal of the rejection of claims 1-4, 7, 8, 10-15, 32-34 and 38 under 35 U.S.C. 112, second paragraph.

4. Rejection of Claims 1-4, 7, 10, 11, 14, 15 and 38 under 35 U.S.C. 102(a)

The Examiner rejected claims 1-4, 7, 10, 11, 14, 15 and 38 under 35 U.S.C. 102(a) as being anticipated by Dowler et al. for the reasons of record. Applicant respectfully traverses this rejection.

Amended claim 1 describes contacting a lipid detector protein with a binding specificity for a product lipid to a solution containing a substrate lipid and lipid phosphatase. In contrast, Dowler et al. describes a method wherein a substrate lipid is incubated with an appropriate enzyme in the presence of a PH domain fused green fluorescent protein. See page 131 lines 24-28. As such, Dowler et al. does not disclose exposing a lipid detector protein to a solution containing a substrate lipid and lipid phosphatase. Accordingly, Dowler et al. does not teach each and every element of the claimed invention, as required to make a proper rejection under 35 USC 102(b). See *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367 (Fed. Cir. 1986).

Furthermore, since claim 38 requires the method of claim 1, this claim is allowable for the same reasons that independent claim 1 is allowable.

In view of the foregoing, Applicant respectfully requests withdrawal of the rejection of claims 1-4, 7, 10, 11, 14, 15 and 38 under 35 U.S.C. 102(a)

5. Common Ownership

The Examiner is thanked for reminding Applicant of its obligation to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made. Applicant asserts that all claims were commonly owned at the time a later invention was made.

6. Rejection of Claim 8 under 35 U.S.C. 103(a)

The Examiner rejected claim 8 under 35 U.S.C. 103(a) as being unpatentable over Dowler et al in view of Goueli et al. for the reasons of record. Applicant respectfully traverses this rejection.

Initially, Applicant would like to point out that to establish a prima facie case of obviousness, it must be shown that each and every one of the claim limitations was suggested or taught by the prior art being relied upon. *In re Royka,* 490 F.2d 981, 180 USPQ 580 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson,* 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). When an independent claim is deemed nonobvious under 35 USC 103, then all claims depending therefrom are nonobvious as well. *In re Fine,* 837 F.2d 1071, 5 USPQ2d 1596 (Fed Cir. 1988).

Applicant respectfully asserts the Examiner has not met this burden. As explained above under the 102(a) rejection, Dowler et al. does not describe contacting a lipid detector protein to a solution containing a substrate lipid of a lipid phosphatase as provided in instant claim 1. Applicant respectfully submits that Goueli et al does not disclose this claim limitation either. Goueli et al discloses a method whereby a reaction solution is spotted onto a binding matrix. See column 14 lines 32-33.

Accordingly, the Examiner has not overcome the aforementioned burden since each and every one of the claim limitations of the instant invention were not taught or suggested by Dowler et al. or Goueli et al., when viewed individually or in combination with one another.

If an independent claim is found to be allowable in an application, all of the claims depending therefrom are allowable as well. Claim 8 depends from claim 1 and therefore, in view of the foregoing arguments in this response, it is also allowable for the same reasons that independent claim 1 is allowable.

As such, Applicant respectfully requests that the Examiner withdraw the rejection of claim 8 under 35 U.S.C. 103(a).

7. Rejection of Claims 12 and 13 under 35 U.S.C. 103(a)

The Examiner rejected claims 12 and 13 under 35 U.S.C. 103(a) as being unpatentable over Dowler et al. in view of Taylor et al. for the reasons of record. Applicant respectfully traverses this rejection.

As previously stated, a prima facie case of obviousness is established only after a showing that each and every one of the claim limitations was suggested or taught by the prior art being relied upon. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974).

Applicant respectfully submits that the Examiner has not met this burden. As explained above under the 102(a) rejection, Dowler et al. does not describe contacting a lipid detector protein to a solution containing a substrate lipid of a lipid phosphatase to determine if the product is present as provided in amended claim 1. Applicant respectfully submits that Taylor et al. does not disclose this claim limitation either. Taylor et al. discloses a method whereby detection of the product is carried out by thin-layer chromatography.

Accordingly, the Examiner has not overcome the aforementioned burden since each and every one of the claim limitations of the instant invention were not taught or suggested by Dowler et al or Taylor et al.

If an independent claim is found to be allowable in an application, all of the claims depending therefrom are allowable as well. Claims 12 and 13 depend from claim 1 and therefore, in view of the foregoing arguments in this response, they are also allowable for the same reasons that independent claim 1 is allowable.

As such, Applicant respectfully requests that the Examiner withdraw the rejection of claims 12 and 13 under 35 U.S.C. 103(a).

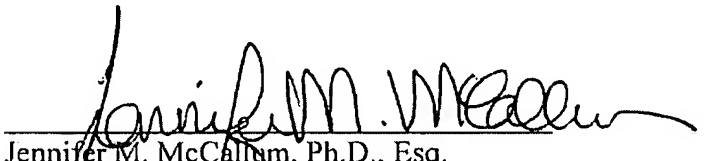
8. Provisional rejection of claims 1-4, 7, 8, 10-12, 14 and 15 on the ground of nonstatutory obviousness-type double patenting

The Examiner provisionally rejected claims 1-4, 7, 8, 10-12, 14 and 15 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-17 of copending Application No. 10/850,833.

Applicant will address this issue by filing a terminal disclaimer upon successful resolution of the other outstanding substantive issues addressed herein.

If the Examiner notes any further matters which would be expedited by a telephonic interview, she is requested to contact Dr. Jennifer M. McCallum at the telephone number listed below.

Respectfully submitted,



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